and/or to a functionally active variant thereof, and also to its use in diagnostics and therapy.

B1 cont.

Replace the paragraph beginning on page 5, line 4 and ending on page 5, line 21 with the following paragraph re-written in clean form:

This object was achieved by identifying T-cell epitopes which in connection with the MHC molecules, and in a particular embodiment with HLA A2.01 MHC molecules, cause, for example, a cytotoxic T-cell response in vivo and in vitro. Said peptides preferably have the sequence ILVPKVSGL (SEQ ID NO: 1), RLVWACVGV (SEQ ID NO: 2), HLFNRAGTV (SEQ ID NO: 3), YLRREQMFV (SEQ ID NO: 4), TLQANKSEV (SEQ ID NO: 5), ILEDWNFGL (SEQ ID NO: 6), SLWLPSEATVYL (SEQ ID NO: 7), NLASSNYFPT (SEQ ID NO: 8), TLTADVMTYI (SEQ ID NO: 9), YLPPVPSKV (SEQ ID NO: 10), YDLQFIFQL (SEQ ID NO: 11), ICWGNQLFV (SEQ ID NO: 12), FYNPDTQRL (SEQ ID NO: 13), MHGDTPTLH (SEQ ID NO: 14), ETTDLYCY (SEQ ID NO: 15), QAEPDRAHYN (SEQ ID NO: 16), SMVTSDAQI (SEQ ID NO: 17). These sequences are part of the L1 and E7 peptides of HPV16. They include the amino acid regions L1 86-94 (5104), L1 123-131 (5106), L1 285-293 (5107), L1 275-283 (5108), L1 238-246 (5109), L1 426-434 (5112), L1 28-39 (2016), L1 311-320 (2017), L1 408-417 (2018), L1 38-47 (2019), L1 396-404 (2020), L1 349-357 (2022), L1 298-306 (27/28), L1 90-98 (9), E7 1-9 (43), E7 18-25 (45) and E7 44-53 (47/48). The names of the relevant epitopes is indicated in brackets.

B2

Replace the paragraph beginning on page 6, line 8 and ending on page 6, line 14 with the following paragraph re-written in clean form:

The present invention therefore relates to a T-cell epitope having an amino acid sequence ILVPKVSGL (SEQ ID NO: 1), RLVWACVGV (SEQ ID NO: 2), HLFNRAGTV (SEQ ID NO: 3), YLRREQMFV (SEQ ID NO: 4), TLQANKSEV (SEQ ID NO: 5), ILEDWNFGL (SEQ ID NO: 6), SLWLPSEATVYL (SEQ ID NO: 7), NLASSNYFPT (SEQ ID NO: 8), TLTADVMTYI (SEQ ID NO: 9), YLPPVPSKV (SEQ ID NO: 10), YDLQFIFQL (SEQ ID NO: 11), ICWGNQLFV (SEQ ID NO: 12), FYNPDTQRL (SEQ ID NO: 13), MHGDTPTLH (SEQ ID NO: 14), ETTDLYCY (SEQ ID NO: 15), QAEPDRAHYN (SEQ ID NO: 16), SMVTSDAQI (SEQ ID NO: 17), and/or to a functionally active variant thereof.

B3

Replace the paragraph beginning on page 6, line 16 and ending on page 6, line 32 with the following paragraph re-written in clean form:

A functionally active variant of ILVPKVSGL (SEQ ID NO: 1), RLVWACVGV (SEQ ID NO: 2), HLFNRAGTV (SEQ ID NO: 3), YLRREQMFV (SEQ ID NO: 4), TLQANKSEV (SEQ ID NO: 5), ILEDWNFGL (SEQ ID NO: 6), SLWLPSEATVYL (SEQ ID NO: 7), NLASSNYFPT (SEQ ID NO: 8), TLTADVMTYI (SEQ ID NO: 9), YLPPVPSKV (SEQ ID NO: 10), YDLQFIFQL (SEQ ID NO: 11), ICWGNQLFV (SEQ ID NO: 12), FYNPDTQRL (SEQ ID NO: 13), MHGDTPTLH (SEQ ID NO: 14), ETTDLYCY (SEQ ID NO: 15), QAEPDRAHYN (SEQ ID NO: 16) or SMVTSDAQI (SEQ ID NO: 17) means a T-cell epitope which, in a T-cell cytotoxicity assay system (see, for example, Examples 2-5 of the present invention), has a cytotoxicity which, compared to the cytotoxicity of ILVPKVSGL (SEQ ID NO: 1), RLVWACVGV (SEQ ID NO: 2), HLFNRAGTV (SEQ ID NO: 3), YLRREQMFV (SEQ ID NO: 4), TLQANKSEV (SEQ ID NO: 5), ILEDWNFGL (SEQ ID NO: 6), SLWLPSEATVYL (SEQ ID NO: 7), NLASSNYFPT (SEQ ID NO: 8), TLTADVMTYI (SEQ ID NO: 9), YLPPVPSKV (SEQ ID NO: 10), YDLQFIFQL (SEQ ID NO: 11), ICWGNQLFV (SEQ ID NO: 12), FYNPDTQRL (SEQ ID NO: 13), MHGDTPTLH (SEQ ID NO: 14), ETTDLYCY (SEQ ID NO: 15), QAEPDRAHYN (SEQ ID NO: 16) or SMVTSDAQI (SEQ ID NO: 17), corresponds to at least the sum of the average of the negative controls and three times the standard deviation, preferably of at least approx. 30%, in particular at least approx. 50% and particularly preferably of at least appox. 80%.

B4

Replace the paragraph beginning on page 6, line 34 and ending on page 7, line 22 with the following paragraph re-written in clean form:

An example of a preferred variant is a T-cell epitope having a sequence homology to ILVPKVSGL (SEQ ID NO: 1), RLVWACVGV (SEQ ID NO: 2), HLFNRAGTV (SEQ ID NO: 3), YLRREQMFV (SEQ ID NO: 4), TLQANKSEV (SEQ ID NO: 5), ILEDWNFGL (SEQ ID NO: 6), SLWLPSEATVYL (SEQ ID NO: 7), NLASSNYFPT (SEQ ID NO: 8), TLTADVMTYI (SEQ ID NO: 9), YLPPVPSKV (SEQ ID NO: 10), YDLQFIFQL (SEQ ID NO: 11), ICWGNQLFV (SEQ ID NO: 12), FYNPDTQRL (SEQ ID NO: 13), MHGDTPTLH (SEQ ID NO: 14), ETTDLYCY (SEQ ID NO: 15), QAEPDRAHYN (SEQ ID NO: 16), or SMVTSDAQI (SEQ ID NO: 17) of at least approx. 65% preferably at least approx. 75% and in particular at least approx. 85% at the amino acid level. Other preferred variants are also T-cell epitopes which are structurally homologous to ILVPKVSGL (SEQ ID NO: 1), RLVWACVGV (SEQ ID NO: 2), HLFNRAGTV (SEQ ID NO: 3), YLRREQMFV (SEQ ID NO: 4), TLQANKSEV (SEQ ID NO: 5), ILEDWNFGL (SEQ ID NO: 6), SLWLPSEATVYL (SEQ ID NO: 7), NLASSNYFPT (SEQ ID NO: 8), TLTADVMTYI (SEQ ID NO: 9), YLPPVPSKV (SEQ ID NO: 10), YDLQFIFQL (SEQ ID NO: 11), ICWGNQLFV (SEQ ID NO: 12), FYNPDTQRL (SEQ ID NO: 13), MHGDTPTLH (SEQ ID NO: 14), ETTDLYCY (SEQ ID NO: 15), QAEPDRAHYN (SEQ ID NO: 16), or SMVTSDAQI (SEQ ID NO: 17). Such epitopes may be found by generating specific T cells against the T-cell epitopes ILVPKVSGL (SEQ ID NO: 1), RLVWACVGV (SEQ ID NO: 2), HLFNRAGTV (SEQ ID NO: 3), YLRREQMFV (SEQ ID NO: 4), TLQANKSEV (SEQ ID NO: 5), ILEDWNFGL (SEQ ID NO: 6), SLWLPSEATVYL (SEQ ID NO: 7), NLASSNYFPT

B5

(SEQ ID NO: 8), TLTADVMTYI (SEQ ID NO: 9), YLPPVPSKV (SEQ ID NO: 10), YDLQFIFQL (SEQ ID NO: 11), ICWGNQLFV (SEQ ID NO: 12), FYNPDTQRL (SEQ ID NO: 13), MHGDTPTLH (SEQ ID NO: 14), ETTDLYCY (SEQ ID NO: 15), QAEPDRAHYN (SEQ ID NO: 16), or SMVTSDAQI (SEQ ID NO: 17) (DeBruijn M.L. et al (1991) Eur. J. Immunol. 21, 2963-70; and DeBruijn M.L. (1992) Eur. J. Immunol. 22, 3013-20) and assaying, for example, synthetically produced peptides of choice for recognition by the peptide-specific T cells (see examples). The T-cell epitopes in particular mean cytotoxic T-cell epitopes. However, noncytotoxic T cells are also known which can likewise recognize MHC I molecules so that the present invention also includes noncytotoxic T-cell epitopes as variant.

B5 cont

Replace the paragraph beginning on page 7, line 31 and ending on page 7, line 39 with the following paragraph re-written in clean form:

In a particular embodiment, a T-cell epitope having an amino acid sequence ILVPKVSGL (SEQ ID NO: 1), RLVWACVGV (SEQ ID NO: 2), HLFNRAGTV (SEQ ID NO: 3), YLRREQMFV (SEQ ID NO: 4), TLQANKSEV (SEQ ID NO: 5), ILEDWNFGL (SEQ ID NO: 6), SLWLPSEATVYL (SEQ ID NO: 7), NLASSNYFPT (SEQ ID NO: 8), TLTADVMTYI (SEQ ID NO: 9), YLPPVPSKV (SEQ ID NO: 10), YDLQFIFQL (SEQ ID NO: 11), ICWGNQLFV (SEQ ID NO: 12), and/or a functionally active variant may be contained in an L1 protein of a different papillomavirus or in a chimeric L1 protein, for example an HPV18L1E7 fusion protein. Such a compound of the invention may have the ability to form CVLPs.

B6 cont.

Replace table 1 on page 29 with the following table re-written in clean form:

Peptide name	Sequence	Relative L1 position
5104	ILVPKVSGL	(86-94) (SEQ ID NO: 1)
5105	SMDYKQTQL	(174-182) (SEQ ID NO: 20)
5106	RLVWACVGV	(123-131) (SEQ ID NO: 2)
5107	HLFNRAGTV	(285-293) (SEQ ID NO: 3)
5108	YLRREQMFV	(275-283) (SEQ ID NO: 4)
5109	TLQANKSEV	(238-246) (SEQ ID NO: 5)
5112	ILEDWNFGL	(426-434) (SEQ ID NO: 6)
5113	TLEDTYRFV	(441-449) (SEQ ID NO: 21)
2016	SLWLPSEATVYL	(28-39) (SEQ ID NO: 7)
2017	NLASSNYFPT	(311-320) (SEQ ID NO: 8)
2018	TLTADVMTYI	(408-417) (SEQ ID NO: 9)
2019	YLPPVPVSKV	(38-47) (SEQ ID NO: 10)
2020	YDLQFIFQL	(396-404) (SEQ ID NO: 11)
2021	FQLCKITLT	(402-410) (SEQ ID NO: 22)
2022	ICWGNQLFV	(349-357) (SEQ ID NO: 12)
2023	KVVSTDEYV	(46-54) (SEQ ID NO: 23)
2024	QLFVTVVDT	(354-362) (SEQ ID NO: 24)
2025	GLQYRVFRI	(93-101) (SEQ ID NO: 25)

B7

Replace table 2 on pages 30, 31, and 32 with the following table re-written in clean form:

Peptid Name	Sequence	relative Position	Epitop-Information
LJ-Peptide			
1	MSLWLPSEATVYLPPVPVSK	(1-20)	(SEQ ID NO: 26)
2	YLPPVPVSKVVSTDEYVART	(12-31)	(SEQ ID NO: 27)
3	STDEYVARTNIYYHAGTSRL	(23-42)	(SEQ ID NO: 28)
4	YYHAGTSRLLAVGHPYFPIK	(34-53)	(SEQ ID NO: 29)
5	VGHPYFPIKKPNNNKILVPK	(45-64)	(SEQ ID NO: 30)
6	NNNKILVPKVSGLQYRVFRI	(56-75)	(SEQ ID NO: 31)
7	GLQYRVFRIHLPDPNKFGFP	(67-86)	(SEQ ID NO: 32)
8	PDPNKFGFPDTSFYNPDTQR	(78-97)	(SEQ ID NO: 33)
9	SFYNPDTQRLVWACVGVEVG	(89-108)	cytotoxic epitope (SEQ ID NO: 34) HLA A24 restr.
10	WACVGVEVGRGQPLGVGISG	(100-119)	(SEQ ID NO: 35)
11	QPLGVGISGHPLLNKLDDTE	(111-130)	(SEQ ID NO: 36)
12	LLNKLDDTENASAYAANAGV	(122-141)	(SEQ ID NO: 37)
13	SAYAANAGVDNRECISMDYK	(133-152)	(SEQ ID NO: 38)
14	RECISMDYKQTQLCLIGCKP	(144-163)	(SEQ ID NO: 39)
15	QLCLIGCKPPIGEHWGKGSP	(155-174)	(SEQ ID NO: 40)
16	GEHWGKGSPCTNVAVNPGDC	(166-185)	(SEQ ID NO: 41)
17	NVAVNPGDCPPLELINTVIQ	(177-196)	(SEQ ID NO: 42)
18	LELINTVIQDGDMVDTGFGA	(188-207)	(SEQ ID NO: 43)
19	DMVDTGFGAMDFTTLQANKS	(199-218)	(SEQ ID NO: 44)
20	FTTLQANKSEVPLDICTSIC	(210-229)	(SEQ ID NO: 45)
21	PLDICTSICKYPDYIKMVSE	(221-240)	(SEQ ID NO: 46)
22	PDYIKMVSEPYGDSLFFYLR	(232-251)	(SEQ ID NO: 47)

B8

23	GDSLFFYLRREQMFVRHLFN	(243-262)	(SEQ ID NO: 48)
24	QMFVRHLFNRAGAVGENVPD	(254-273)	(SEQ ID NO: 49)
25	GAVGENVPDDLYIKGSGSTA	(265-284)	(SEQ ID NO: 50)
26	YIKGSGSTANLASSNYFPTP	(276-295)	(SEQ ID NO: 51)
27	ASSNYFPTPSGSMVTSDAQI	(287-306)	**T-helper epitope** (SEQ ID NO: 52)
28	SMVTSDAQIFNKFYWLQRAQ	(298-317)	**T-helper epitope** (SEQ ID NO: 53)
29	KPYWLQRAQGHNNGICWGNQ	(309-328)	(SEQ ID NO: 54)
30	NNGICWGNQLFVTVVDTTRS	(320-339)	(SEQ ID NO: 55)
31	VTVVDTTRSTNMSLCAAIST	(331-350)	(SEQ ID NO: 56)
32	MSLCAAISTSETTYKNTNFK	(342-361)	(SEQ ID NO: 57)
33	TTYKNTNFKEYLRHGEEYDL	(353-372)	(SEQ ID NO: 58)
34	LRHGEEYDLQFIFQLCKITL	(364-383)	(SEQ ID NO: 59)
35	IFQLCKITLTADVMTYIHSM	(375-394)	(SEQ ID NO: 60)
36	DVMTYIHSMNSTILEDWNFG	(386-405)	(SEQ ID NO: 61)
37	TILEDWNFGLQPPPGGTLED	(397-416)	(SEQ ID NO: 62)
38	PPPGGTLEDTYRFVTSQAIA	(408-427)	(SEQ ID NO: 63)
39	RFVTSQAIACQKHTPPAPKE	(419-438)	(SEQ ID NO: 64)
40	KHTPPAPKEDPLKKYTFWEV	(430-449)	(SEQ ID NO: 65)
41	LKKYTFWEVNLKEKFSADLD	(441-460)	(SEQ ID NO: 66)
42	KEKFSADLDQFPLGRKFLLQ	(452-471)	(SEQ ID NO: 67)
43	PLGRKFLLQAGMHGDTPTLH	(463-482)	**cytotoxic epitope HLA A1 restr.** (SEQ ID NO: 68)

B8 cont

E7 Peptides

44	MHGDTPTLHEYMLDLQPETT	(1-20)	(SEQ ID NO: 69)
45	MLDLQPETTDLYCYEQLNDS	(12-31)	**cytotoxic epitope HLA A1 restr.** (SEQ ID NO: 70)
46	YCYEQLNDSSEEEDEIDGPA	(23-42)	(SEQ ID NO: 71)
47	EEDEIDGPAGQAEPDRAHYN	(34-53)	**cytotoxic epitope HLA A1 restr.** (SEQ ID NO: 72)
48	AEPDRAHYNIVTFCCKCDST	(45-64)	**cytotoxic epitope HLA A1 restr.** (SEQ ID NO: 73)
49	TFCCKCDSTLRLCVQSTHVD	(56-75)	(SEQ ID NO: 74)
50	LCVQSTHVDIRTLEDLLMGT	(67-86)	(SEQ ID NO: 75)
51	TLEDLLMGTLGIVCPICSQKP	(78-97)	(SEQ ID NO: 76)

Influenza control peptide

52	KEYLRHGEEGILGFVFTLCK	(SEQ ID NO: 77)

Replace the paragraph beginning on page 36, line 26 and ending on page 36, line 35 with the following paragraph re-written in clean form:

B9

Result: Fig. 4 shows that PBMCs incubated with peptides 43, 47 and 48, but not PBMCs incubated with the remaining peptides, effected restimulation of CVLP-stimulated T cells. Peptide 43 contains the 9mer peptide of the sequence MHGDTPTLH (SEQ ID NO: 14), and the two overlapping peptides 47 and 48 contain the 10mer peptide of the sequence QAEPDRAHYN (SEQ ID NO: 16), which in each case have been described as HLA A1-binding peptides in Kast et al. (supra), but for which it has been impossible so far to carry out a functional detection.

Replace the paragraph beginning on page 37, line 23 and ending on page 37, line 29 with the following paragraph re-written in clean form:

B10

Result: Fig. 5 shows that PBMCs incubated with peptides 27 and 28, but not PBMCs incubated with the remaining peptides, effected restimulation of CVLP-stimulated T cells. The two overlapping peptides 27 and 28 contain the peptide of the sequence SMVTSDAQI (SEQ ID NO: 17) so that the actually recognized peptide essentially must include this sequence.

Replace the paragraph beginning on page 38, line 21 and ending on page 38, line 30 with the following paragraph re-written in clean form:

B11

Result: Fig. 6 shows that PBMCs incubated with peptide pools E and 6, but not PBMCs incubated with the remaining peptide pools, effected restimulation of CVLP-stimulated T cells. Peptide pools E and 6 both contain peptide 45 which thus is in all probability responsible for restimulation of CVLP-stimulated T cells. Peptide 45 in turn contains peptide ETTDLYCY (SEQ ID NO: 15) which has been described as HLA A1-binding peptide by Kast et al. (supra), but for which it has been impossible so far to carry out a functional detection.

Replace the paragraph beginning on page 39, line 5 and ending on page 39, line 14 with the following paragraph re-written in clean form:

B12

Result: Fig. 7 shows that PBMCs incubated with peptide pools A and 2, but not PBMCs incubated with the remaining peptide pools, effected restimulation of CVLP-stimulated T cells. Peptide pools A and 2 both contain peptide 9 which thus is in all probability responsible for restimulation of CVLP-stimulated T cells. The prediction according to